

AMENDMENTS TO THE CLAIMS/LISTING OF CLAIMS

Please enter the following amendments without prejudice or disclaimer. This listing of claims will replace all prior versions, and listings, of claims in the application.

In the claims:

1-23. (Canceled)

24. (Currently amended) A method of reducing or moderating a postprandial rise in plasma glucose in a mammal comprising administering to said mammal in need of reducing or moderating a postprandial rise in plasma glucose an amylin agonist analogue in an amount effective to reduce or moderate a postprandial rise in plasma glucose, wherein the amylin agonist analogue is a peptide having [[an]] **the** amino acid sequence selected from the group consisting of

- a) ¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵Pro-I₁-Leu-J₁-Pro-³⁰Thr-K₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z
(SEQ ID NO:42)

wherein

A₁ is Lys, Ala, Ser or hydrogen;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr;

I₁ is Ile, Val, Ala or Leu;

J₁ is Ser, Pro, Leu, Ile or Thr;

K₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are

chemically bonded to each other to form an intramolecular linkage,

wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy, and

provided that when

- (i) A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Val, J₁ is Pro and K₁ is Asn; or
- (ii) A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Asn, G₁ is Asn, H₁ is Leu, I₁ is Val, J₁ is Ser and K₁ is Asn;

then one or more of A₁ to K₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy;

- b) ¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵I₁-J₁-Leu-Pro-Pro-³⁰Thr-K₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z
(SEQ ID NO:44)

wherein

A₁ is Lys, Ala, Ser or hydrogen;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr;

I₁ is Ala or Pro;

J₁ is Ile, Val, Ala or Leu;

K₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage,

wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and

provided that when

A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val and K₁ is Asn (SEQ ID NO:41),

then one or more of A₁ to K₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy;

- c) ¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵Pro-I₁-Leu-Pro-Pro-³⁰Thr-J₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:45)

wherein

A₁ is Lys, Ala, Ser or hydrogen;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr;

I₁ is Ile, Val, Ala or Leu

J₁ is Asn, Asp or Gln; and

X and Y are independently selected residues having side chains which are

chemically bonded to each other to form an intramolecular linkage wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or

aralkyloxy;
provided that when

A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Val and J₁ is Asn (SEQ ID NO:41),

then one or more of A₁ to J₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and

- d) ¹A₁-X-Asn-Thr-⁵Ala-Thr-[[X]]Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁Asn-H₁-Gly-²⁵I₁-J₁-Leu-K₁-L₁-³⁰Thr-M₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:31)

wherein

A₁ is Lys, Ala, Ser, Hydrogen or acetylated Lys;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr,

I₁ is Ala or Pro;

J₁ is Ile, Val, Ala or Leu;

K₁ is Ser, Pro, Leu, Ile or Thr;

L₁ is Ser, Pro or Thr;

M₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is an amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy;

provided that

- (a) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Phe, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Ser, and M₁ is Asn (SEQ ID NO:46);
- (b) when A₁ is Lys, B₁ is Ala, C₁ is Ile, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Pro, and M₁ is Asn (SEQ ID NO:47);
- (c) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Thr, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Pro, and M₁ is Asn (SEQ ID NO:48);
- (d) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val, K₁ is Pro, L₁ is Pro, and M₁ is Asn (SEQ ID NO:41);
- (e) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Asn, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val, K₁ is Ser, L₁ is Pro and M₁ is Asn (SEQ ID NO:43); or
- (f) when A₁ is Lys, B₁ is Thr, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is His, H₁ is Leu, I₁ is Ala, J₁ is Ala, K₁ is Leu, L₁ is Pro and M₁ is Asp (SEQ ID NO:49);

then one or more of any of A₁ to M₁ is not an L-amino acid and Z is not amino.

25. (Previously presented) The method of claim 24 wherein the amylin agonist analogue has the following amino acid sequence:

¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-
G₁-Asn-H₁-G₁ly-²⁵Pro-I₁-Leu-Pro-J₁-³⁰Thr-K₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:40)
wherein

- A₁ is Lys, Ala, Ser or Hydrogen;
- B₁ is Ala, Ser or Thr;
- C₁ is Val, Leu or Ile;
- D₁ is His or Arg;

E₁ is Ser or Thr;
F₁ is Ser, Thr, Gln or Asn;
G₁ is Asn, Gln or His;
H₁ is Phe, Leu or Tyr;
I₁ is Ile, Val, Ala or Leu;
J₁ is Ser, Pro or Thr;
K₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is an amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkylloxy, aryloxy or aralkyloxy; and provided that when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Val, J₁ is Pro, and K₁ is Asn; then one or more A₁ to K₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkylloxy, aryloxy or aralkyloxy.

26. (Previously presented) The method of claim 24 wherein the amylin agonist analogue has the following amino acid sequence:

¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵Pro-I₁-Leu-J₁-Pro-³⁰Thr-K₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:42)
wherein

A₁ is Lys, Ala, Ser or hydrogen;
B₁ is Ala, Ser or Thr;
C₁ is Val, Leu or Ile;
D₁ is His or Arg;
E₁ is Ser or Thr;
F₁ is Ser, Thr, Gln or Asn;
G₁ is Asn, Gln or His;
H₁ is Phe, Leu or Tyr;
I₁ is Ile, Val, Ala or Leu;

J₁ is Ser, Pro, Leu, Ile or Thr;

K₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy, and provided that when

(a) A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Val, J₁ is Pro and K₁ is Asn; or

(b) A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Asn, G₁ is Asn, H₁ is Leu, I₁ is Val, J₁ is Ser and K₁ is Asn;

then one or more of A₁ to K₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy.

27. (Previously presented) The method of claim 24 wherein the amylin agonist analogue has the following amino acid sequence:

¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵I₁-J₁-Leu-Pro-Pro-³⁰Thr-K₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:44)
wherein

A₁ is Lys, Ala, Ser or hydrogen;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr;

I₁ is Ala or Pro;

J₁ is Ile, Val, Ala or Leu;

K₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and provided that when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val and K₁ is Asn (SEQ ID NO:41); then one or more of A₁ to K₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy.

28. (Previously presented) The method of claim 24 wherein the amylin agonist analogue has the following amino acid sequence:

¹A₁-X-Asn-Thr-⁵Ala-Thr-Y-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-²⁰F₁-G₁-Asn-H₁-Gly-²⁵Pro-I₁-Leu-Pro-Pro-³⁰Thr-J₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID NO:45)
wherein

A₁ is Lys, Ala, Ser or hydrogen;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr;

I₁ is Ile, Val, Ala or Leu

J₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy; and provided that when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is

Leu, I₁ is Val and J₁ is Asn (SEQ ID NO:41); then one or more of A₁ to J₁ is a D-amino acid and Z is selected from the group consisting of alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkyloxy, aryloxy or aralkyloxy.

29. (Previously presented) The method of claim 24 wherein said amylin agonist analogue is any one of ¹⁸Arg^{25,28}Pro-h-amylin (SEQ ID NO:3), des-¹Lys¹⁸Arg^{25,28}Pro-h-amylin (SEQ ID NO:6), ^{25,28,29}Pro-h-amylin (SEQ ID NO:1), des-¹Lys^{25,28,29}Pro-h-amylin (SEQ ID NO:10), ¹⁸Arg^{25,28,29}Pro-h-amylin (SEQ ID NO:8), des-¹Lys¹⁸Arg^{25,28,29}Pro-h-amylin (SEQ ID NO:9), ²⁵Pro²⁶Val^{28,29}Pro-h-amylin (SEQ ID NO:7), or des-¹Lys²⁵Pro²⁶Val^{28,29}Pro-h-amylin (SEQ ID NO:38).

30. (Previously presented) The method of claim 24 wherein the amylin agonist analogue is ^{25,28,29}Pro-h-amylin (SEQ ID NO:1).

31-37. (Canceled)

38. (Previously presented) The method of claim 24 wherein the mammal has diabetes.

39. (Previously presented) The method of claim 38 wherein the diabetes is type 1.

40. (Previously presented) The method of claim 38 wherein the diabetes is type 2.

41. (Previously presented) The method of claim 25 wherein the mammal has diabetes.

42. (Previously presented) The method of claim 41 wherein the diabetes is type 1.

43. (Previously presented) The method of claim 41 wherein the diabetes is type 2.

44. (Previously presented) The method of claim 26 wherein the mammal has diabetes.

45. (Previously presented) The method of claim 44 wherein the diabetes is type 1.

46. (Previously presented) The method of claim 44 wherein the diabetes is type 2.

47. (Previously presented) The method of claim 27 wherein the mammal has diabetes.

48. (Previously presented) The method of claim 47 wherein the diabetes is type 1.
49. (Previously presented) The method of claim 47 wherein the diabetes is type 2.
50. (Previously presented) The method of claim 28 wherein the mammal has diabetes.
51. (Previously presented) The method of claim 50 wherein the diabetes is type 1.
52. (Previously presented) The method of claim 50 wherein the diabetes is type 2.
53. (Previously presented) The method of claim 30 wherein the mammal has diabetes.
54. (Previously presented) The method of claim 53 wherein the diabetes is type 1.
55. (Previously presented) The method of claim 53 wherein the diabetes is type 2.
56. (Currently amended) The method of claim 24 wherein the amylin agonist analogue has the following amino acid sequence:

¹A₁-X-Asn-Thr-⁵Ala-Thr-**[(X)]Y**-Ala-Thr-¹⁰Gln-Arg-Leu-B₁-Asn-¹⁵Phe-Leu-C₁-D₁-E₁-
²⁰F₁-G₁Asn-H₁-Gly-²⁵I₁-J₁-Leu-K₁-L₁-³⁰Thr-M₁-Val-Gly-Ser-³⁵Asn-Thr-Tyr-Z (SEQ ID
NO:31)

wherein

A₁ is Lys, Ala, Ser, Hydrogen or acetylated Lys;

B₁ is Ala, Ser or Thr;

C₁ is Val, Leu or Ile;

D₁ is His or Arg;

E₁ is Ser or Thr;

F₁ is Ser, Thr, Gln or Asn;

G₁ is Asn, Gln or His;

H₁ is Phe, Leu or Tyr,

I₁ is Ala or Pro;

J₁ is Ile, Val, Ala or Leu;

K₁ is Ser, Pro, Leu, Ile or Thr;

L₁ is Ser, Pro or Thr;

M₁ is Asn, Asp or Gln;

X and Y are independently selected residues having side chains which are chemically bonded to each other to form an intramolecular linkage, wherein said intramolecular linkage comprises a disulfide bond, a lactam or a thioether linkage; and Z is an amino, alkylamino, dialkylamino, cycloalkylamino, arylamino, aralkylamino, alkylloxy, aryloxy or aralkyloxy; and provided that

(a) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Phe, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Ser, and M₁ is Asn (SEQ ID NO:46);

(b) when A₁ is Lys, B₁ is Ala, C₁ is Ile, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Pro, and M₁ is Asn (SEQ ID NO:47);

(c) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Thr, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Ala, J₁ is Ile, K₁ is Ser, L₁ is Pro, and M₁ is Asn (SEQ ID NO:48);

(d) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val, K₁ is Pro, L₁ is Pro, and M₁ is Asn (SEQ ID NO:41);

(e) when A₁ is Lys, B₁ is Ala, C₁ is Val, D₁ is His, E₁ is Ser, F₁ is Asn, G₁ is Asn, H₁ is Leu, I₁ is Pro, J₁ is Val, K₁ is Ser, L₁ is Pro and M₁ is Asn (SEQ ID NO:43); or

(f) when A₁ is Lys, B₁ is Thr, C₁ is Val, D₁ is Arg, E₁ is Ser, F₁ is Ser, G₁ is His, H₁ is Leu, I₁ is Ala, J₁ is Ala, K₁ is Leu, L₁ is Pro and M₁ is Asp (SEQ ID NO:49);

then one or more of any of A₁ to M₁ is not an L-amino acid and Z is not amino.

57. (Previously presented) The method of claim 56 wherein the mammal has diabetes.

58. (Previously presented) The method of claim 57 wherein the diabetes is type 1.

59. (Previously presented) The method of claim 57 wherein the diabetes is type 2.

60-69. (Canceled)